Conferences and Reviews

Increased Erythrocyte Sedimentation Rate and a Splenic Mass
Clinicopathologic Conference

Discussants
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This discussion was selected from the weekly Grand Rounds in the Department of Medicine, University of Washington School of Medicine, Seattle. Taken from a transcription, it has been edited by Jonathan G. Drachman, MD, Chief Medical Resident; Henry Rosen, MD, Professor and Associate Chair; and Paul G. Ramsey, MD, Professor and Chair of the Department of Medicine.

Case Presentation

JONATHAN G. DRACHMAN, MD*: A 34-year-old man was referred to the infectious diseases clinic at the University of Washington Medical Center for a second opinion and evaluation of a splenic mass associated with an increased erythrocyte sedimentation rate (ESR).

In 1987 the patient was found to have an ESR of 85 mm per hour during routine physical examination and laboratory evaluation for insurance screening. Repeated studies confirmed the abnormal result (ESR range, 60 to 105 mm per hour). The patient remained asymptomatic, and no abnormalities were detected on the physical examination. Additional workup revealed moderate anemia (hematocrit, 0.32 [32%]) with hypochromic, microcytic erythrocytes. A bone marrow biopsy revealed normal iron stores, consistent with anemia of chronic disease.

No further evaluation was done until the patient established care with a local internist in May 1992. At that time, the patient admitted to having occasional headaches and fatigue, but otherwise claimed to be in good health. He did not have fevers, night sweats, rash, arthralgias, myalgias, lymphadenopathy, or abdominal pain. He was not taking any medications. There was no history of recreational drug use. He was a nonsmoker and drank alcohol only rarely. He was born in Boise, Idaho, and moved to Seattle in his early 20s. His job as an international businessman required extensive foreign travel to Europe (France, Italy, Spain), South America (Argentina, Ecuador, Peru, Chile), and Asia (Hong Kong, Japan, China, Thailand). He was married and lived with his wife and two cats in the Seattle area.

An enlarged spleen was then palpable in the left upper quadrant of the abdomen; the physical examination otherwise showed no abnormalities. An extensive workup followed. A tuberculin skin test using intermediate-strength purified-protein derivative was negative (with positive controls). Hematologic studies showed a hematocrit of 0.36 (36%), a leukocyte count of 8×10^9 per liter (8,000 per mm^3) with a normal differential (no eosinophilia), an ESR of 95 mm per hour, and a fibrinogen level of 720 ng per dl. Serum electrolyte, creatinine, and liver function test values were unremarkable. Blood cultures were negative. Bone marrow aspiration and biopsy were done, revealing no bacterial, fungal, or mycobacterial organisms using appropriate stains and cultures; there was no evidence of neoplasia in the marrow. Tests for antinuclear antibodies and rheumatoid factor were normal. Serum protein electrophoresis showed hypergammaglobulinemia without a spike (consistent with inflammation). Assays for cryoglobulins and cryofibrinogens were negative.

A chest radiograph showed a slightly elevated left hemidiaphragm and no lung infiltrates, nodules, or mediastinal adenopathy. An abdominal computed tomographic (CT) scan (Figure 1) demonstrated a large splenic mass ($9 \times 8 \times 9$ cm) with scattered calcifications and two small (1 to 2 cm) noncalcified hypodense lesions. The liver and kidneys were normal, and no abdominal adenopathy was identified.

The patient was referred to an infectious disease consultant, who considered the diagnosis of schistosomiasis, given the splenic mass and travel history. Tests of stool and urine specimens were negative for ova and parasites. An intravenous pyelogram was normal, and rectal biopsy results also did not show schistosomiasis.

The splenic masses, increased ESR, and anemia of chronic disease remained a mystery. A splenectomy was recommended for diagnosis and possible therapy. The pa-

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ABBREVIATIONS USED IN TEXT
CT = computed tomographic
ESR = erythrocyte sedimentation rate

tient was referred to this institution for a second opinion as to the cause of the illness and the necessity for this operation.

Discussion

JAN V. HIRSCHMANN, MD*: The patient's travel history looms as an important element to consider in trying to uncover the correct diagnosis. The other salient points include an increased ESR and anemia of chronic disease, both present for at least five years; splenic masses with evidence on CT scan of scattered calcifications, but without contents of water density to suggest cystic structures; and an absence of symptoms.

An impulse to cut away what seems inessential is known as Ockham's (or Occam's) razor, named after a 14th-century English religious philosopher, William of Ockham. Also called the law of parsimony, this concept states that entities should not be multiplied needlessly, or in other words, that the simplest of competing theories is preferable. The "razor" excises unnecessary information or concepts. Accordingly, I will assume that the splenic masses and the long-standing laboratory abnormalities are related. Ockham's razor, however, has limitations. Discerning what is superfluous, for example, may be difficult. Furthermore, although the law of parsimony is usually reasonable in young, otherwise healthy persons, when people age, become chronically ill, or have immunodeficiency, several diseases often coexist, and attempting to explain all clinical findings by a single disorder may be misleading. A recent editorial reflects this problem in its title, "Is Occam's razor disposable?"[1] Nevertheless, in considering the young, robust patient in the present case, I will employ this sharp instrument.

What information does a review of the patient's long-standing anemia and an elevated ESR provide? The anemia of chronic disease,[2] once called "chronic, simple anemia," has several aliases, including "anemia of chronic disorders"[3] and "anemia of inflammation,"[4] proposed because inflammation seems present in most, perhaps all, of the underlying conditions. The important features of this disorder include a decrease in both serum iron levels and total iron-binding capacity, with the saturation typically 10% to 20%, compared with the normal of about 20% to 45%. In about a fifth of patients with anemia of chronic disease, however, the saturation is below 10%—a level that creates confusion with iron-deficiency anemia—but the serum ferritin level, which is low in iron deficiency, is normal or elevated. Furthermore, iron is present in bone marrow aspirates, which also reveal that the iron-containing nucleated erythrocytes (sideroblasts) constitute less than 30% of the total number of nucleated erythrocytes, compared with the normal of 30% to 50%. The decreased number of iron granules in the erythrocyte precursors despite the abundant amount of marrow iron suggests that the major pathogenic factor is the imprisonment of iron in the marrow. As is so often the case, such a simple explanation is misleading, and the problem, instead, is diminished production caused by the actions of cytokines.[5] Interleukin-1, tumor necrosis factor, and interferon alfa, produced during inflammation, inhibit erythroid precursors, decrease erythropoietin production, and impair iron release. High-dose erythropoietin, however, can overcome these effects and correct the anemia.[5]

Anemia of chronic disease is commonly normochromic and normocytic. In about 50% of patients, however, the mean corpuscular hemoglobin concentration is low, indicating hypochromia, and in 20% to 30% the mean corpuscular volume is reduced, signifying microcytosis.[6,7] The hematocrit usually becomes stable at a level above 0.30 after about two months, but in 20% it is less than 0.25. A review of the records of patients admitted to a hospital with this type of anemia found that 35% had acute or chronic infections, 20% had malignant neoplasms, 15% had renal insufficiency, and 5% had rheumatic diseases.[7] Miscellaneous problems constituted the remaining 25%; among these were several with chronic noninflammatory disorders, such as congestive heart failure and obstructive lung disease, infirmities not traditionally associated with this type of anemia.

The increased ESR in this case is another nonspecific finding. Originally developed in 1918 as a test for pregnancy, the ESR measures the distance in millimeters that erythrocytes fall in a glass tube in one hour.[8,9] Being negatively charged, erythrocytes repel each other and settle slowly. Certain plasma proteins, especially fibrinogen but also the globulins, are positively charged, promote

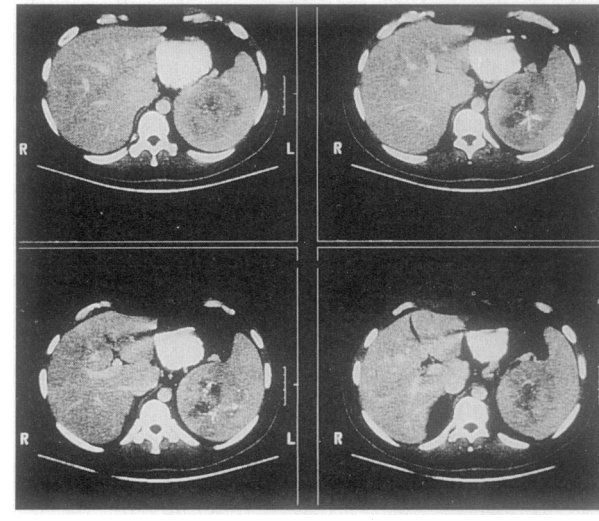

Figure 1.—The abdominal computed tomograms of sequential cuts through the abdomen demonstrate a single, large hypodense mass in the spleen with scattered calcification. The stomach is partially opacified by an oral contrast medium; the liver and kidneys appear normal, and no abdominal adenopathy is visible.

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erythrocyte aggregation (or rouleaux formation), and increase the ESR above the normal rate of about 20 mm per hour. In a large group of outpatients, when the ESR was between 75 and 99 mm per hour, which occurred in about 4%, the underlying disorders were infection in 15%; renal disease, rheumatic disorders, and malignant lesions in 10% each; and miscellaneous illnesses in 5%; the cause was unknown in 50%.[10] Once the rate exceeds 100 mm per hour, however, a diagnosis is nearly always evident: infection, usually acute, in about 35%; cancer, usually metastatic, in 25%; rheumatic disorders in 15%; renal disease in 5%; miscellaneous conditions in 15%; and unknown in only about 5%.[10-15] A markedly increased ESR, like anemia of chronic disease, is compatible with many disorders, but most strongly implies an infectious or malignant cause, a conclusion that does not substantially advance the primary diagnostic considerations of splenic masses. Yet these laboratory findings are, curiously, a crux in this case, for they indicate that the patient has probably had his splenic process for at least five years, an important point in exploring the possible diagnoses.

Among possible infections, the most arresting feature in this patient is his extensive travel history, suggesting especially a parasitic disorder—several of which commonly cause splenomegaly—including malaria, schistosomiasis, toxoplasmosis, and leishmaniasis (kala-azar). These disorders produce enlarged spleens, sometimes to gargantuan proportions, but the pathologic findings are granulomas—as an inflammatory response to the microorganisms—not masses.[16] An additional mechanism in schistosomiasis is liver infestation causing portal hypertension and, consequently, congestive splenomegaly.[17] Echinococcal infection, however, can cause splenic masses, usually associated with similar masses in the liver, but these are cysts with contents of water density, not the findings on CT in this patient.

Four types of chronic bacterial infections merit brief scrutiny. Brucellosis develops from ingesting organisms originating in cattle, sheep, goats, swine, and dogs; in some patients splenic abscesses may be present for years,[18] but they produce symptoms, such as fever and weight loss, at least intermittently. *Mycobacterium tuberculosis* can infect the spleen, but the lack of organ involvement elsewhere in this patient, especially in the lungs, is unusual, and the negative tuberculin test despite intact cutaneous hypersensitivity to other antigens nearly exonerates the presence of active infection,[19] although it does not completely exclude it. Tertiary syphilis can result in a splenic gumma, a mass of granulomatous inflammation, but this is a rare manifestation of *Treponema pallidum* infection.[20] Melioidosis, an infection with *Pseudomonas pseudomallei*, a gram-negative bacillus found in Asia, can be acute or chronic and, like tuberculosis, may be latent for years. Although infection of the spleen occurs, most patients have a history of a preceding febrile disease, usually with lung involvement, and roentgenographic evidence of a current pulmonary inflammatory process.[21]

In theory, an untreated splenic abscess could partially resorb, leaving a mass with calcifications, but several factors militate against such a diagnosis. Patients with splenic abscesses, about 30% of whom are immunocompromised, typically have an obvious predisposing factor, most commonly (about 55% of cases) an infection causing bacteremia, such as endocarditis or urinary tract sepsis. In about 20% the underlying process is trauma and in 10% hemolytic anemia, wherein splenic congestion with destroyed erythrocytes causes ischemia or hemorrhage. In both these settings, a transient, asymptomatic bacteremia presumably infects hematomas, necrotic tissue, or ischemic foci, against which local defense mechanisms are ineffective. In 5% of cases of splenic abscess, the infection spreads from a contiguous, usually intra-abdominal, area of suppuration. In only 10% of cases is no predisposing factor evident.[22,23] The responsible organisms, such as *Staphylococcus aureus*, streptococci, and *Salmonella* and *Candida* species, are typically aggressive, and, not surprising, most patients are acutely ill, with symptoms present for one to three weeks. About 90% are febrile, 60% have generalized or left upper quadrant abdominal pain, and 90% have leukocytosis. The absence of these characteristics in this patient makes splenic abscess unlikely.

With no infectious cause providing a credible diagnosis, neoplasms should be considered. Splenic metastases are detectable in about 2% to 9% of cancers at autopsy,[24] the most frequent primary sites being the lungs, breasts, and skin (malignant melanoma). In a nonsmoker with a normal chest film, an occult bronchogenic carcinoma is highly improbable. Breast cancers can develop in men, but only 6% occur in patients younger than 40, the primary cancer is usually obvious on physical examination, and this cancer, in men as in women, rarely presents as a metastatic cancer of unknown primary.[25] Malignant melanomas deserve careful consideration, however. With this protean tumor, the interval between the discovery of the primary and the subsequent appearance of a metastasis is sometimes decades.[26] It is conceivable that the patient previously had a skin lesion not recognized as a melanoma that was removed or destroyed by cautery, cryosurgery, or other trauma. An alternative scenario is that the primary tumor disappeared on its own. In an extensive review of the spontaneous regression of cancer, malignant melanoma accounted for 11% of the reported cases, the third most frequent cause behind renal cell carcinoma and neuroblastoma in children.[27] Nevertheless, splenic metastases, even in patients with malignant melanoma, usually occur with obvious, widespread disease elsewhere.

Primary benign tumors of the spleen include hamartoma, hemangioma, or lymphangioma.[28] None are likely to have the CT appearance seen in this patient or to cause the anemia of chronic disease and an increased ESR. Primary splenic cancers, which are rare, apparently arise from vascular endothelium. Although some authorities have separated angiosarcomas from hemangioendotheliomas,[29] others label all such vascular tumors angiosarcomas.[16,30,31] These neoplasms are usually not just malignant, but virulent. They are nearly always aggressive, often

spreading locally or metastasizing early to lymph nodes, lung, or liver. Few patients survive more than a year. Another splenic neoplasm, malignant fibrous histiocytoma, also displays virulence.[30] These clinical features make primary splenic cancer an unlikely candidate for an asymptomatic disease that has been present for at least five years.

Another consideration is a malignant lymphoreticular disorder. Primary splenic Hodgkin's disease is rare, but disease confined to the spleen occurs in about 1% to 2% of patients with non-Hodgkin's lymphoma.[32-34] The gross pathologic appearance may be homogeneous enlargement, miliary nodules 1 to 5 mm in diameter, or masses greater than 2 cm in diameter. Because non-Hodgkin's lymphoma can cause anemia of chronic disease and an increased ESR, produce no symptoms, and produce masses in the spleen, even with areas of calcification,[35] this diagnosis is plausible. With non-Hodgkin's lymphomas, however, the kinds that can be asymptomatic do not cause splenic masses, and the type that causes masses (large-cell lymphoma) is an aggressive, symptomatic cancer highly unlikely to be latent for five years.[36]

I have surveyed the possibilities of both infections and neoplasms and found no plausible diagnosis. Is there another way to bring together tumors and inflammation? Several inflammatory disorders have features like neoplasms; two that can involve the spleen are giant lymph node hyperplasia (Castleman's disease) and inflammatory pseudotumor. Castleman's disease typically causes obvious lymph node enlargement, especially in the mediastinum. Although multicentric disease can result in splenic masses, the absence of lymphadenopathy on physical examination, chest radiograph, and abdominal CT scan makes this diagnosis unlikely.[37] Inflammatory pseudotumors are masses of unknown cause characterized by nonspecific inflammation consisting of lymphocytes, plasma cells, histiocytes, and fibrosis in varying combinations.[38] Although described more frequently in the lungs and orbits, in 15 reported cases the spleen was involved. The patients, whose ages ranged from 19 to 75, had various presentations, including fever, anemia, and splenomegaly; some had no symptoms. In one patient splenic calcification was apparent on the CT scan.[39] Inflammatory pseudotumors are single or multiple, sharply demarcated or poorly circumscribed masses, often of impressive dimensions (as much as 12.7 cm in diameter). This disorder could explain all the elements in this case, including the lack of symptoms, the lengthy duration, the laboratory abnormalities, and the CT findings. I therefore declare that the diagnosis is inflammatory pseudotumor of the spleen.

Before concluding, however, I shall address the question of splenectomy. This procedure has important complications, both in the perioperative period and afterwards. The risks of immediate problems seem related, in part, to the reason for the operation and the age of the patient, with complications occurring more frequently in older patients.[40] When performed for trauma or incidentally during a surgical procedure for another purpose, such as gastrectomy, the morbidity is about 30% and the mortality 15%. When the reason is an underlying hematologic disease, such as hemolytic anemia, immune thrombocytopenia, or leukemia, splenectomy incurs a morbidity of about 25% and a mortality of 10%.[41-43] Perhaps the most analogous situation to that of our patient is splenic removal during staging laparotomy for Hodgkin's disease, a disorder primarily of the young, in which the morbidity is about 10% and the mortality 5%. The complications are primarily respiratory and infectious, but thromboembolic phenomena, including leg vein thrombi, pulmonary emboli, and mesenteric venous occlusion occur in about 1% to 2% of patients, presumably related to the thrombocytosis that develops following splenectomy.

Splenic removal also imposes long-term risks. In addition to its main function of weeding out the weak, misshapen, and aged erythrocytes, the spleen removes particulate matter, including microorganisms, from the circulation. It also produces immunoglobulin M and cytokines in response to acute infections and synthesizes components of the alternative pathway of complement activation. The absence of these filtering and immunologic functions predisposes asplenic patients to an apparent increase in the frequency and severity of certain infectious diseases. Those caused by intraerythrocytic parasites like malaria seem more virulent. The best information exists for *Babesia microti*,[44] an organism that infects erythrocytes and is transmitted to humans by the same tick, *Ixodes dammini*, that transmits Lyme disease. This parasite also lives in the species of mice that *Borrelia burgdorferi* infects. Babesiosis occurs primarily in certain coastal areas of the Northeast, where it can cause inapparent infections. Symptomatic disease may be more frequent in patients without spleens in whom fever, myalgias, hemolytic anemia, and renal failure have occurred. Because this organism is difficult to treat and may be lethal, asplenic patients should probably avoid certain areas of the Northeast. Indeed, avoiding these areas of the Northeast is prudent for people *with* spleens.

Another infectious agent seemingly more virulent in asplenic hosts is a gram-negative bacillus recently named *Capnocytophaga canimorsus* (previously designated DF-2).[45] A part of the normal mouth flora of dogs, it can cause severe infection following dog bites; in patients without spleens, bacteremia with disseminated intravascular coagulation and peripheral gangrene has developed. Occasionally the disease has followed exposure to cats, making these two domestic beasts possibly dangerous for asplenic humans.

Although some authors express concern about *Neisseria meningitidis* (meningococcus) and *Haemophilus influenzae*, infections from these organisms may not be more frequent or severe in asplenic hosts. Clearly the most serious consideration is *Streptococcus pneumoniae*. Fatal pneumococcal sepsis following splenectomy occurs in children with a frequency of about 1 case per 300 patient-years.[46] If this rate were sustained during the adult years, the risk of this infection would obviously be substantial over the lifetime of someone undergoing splenec-

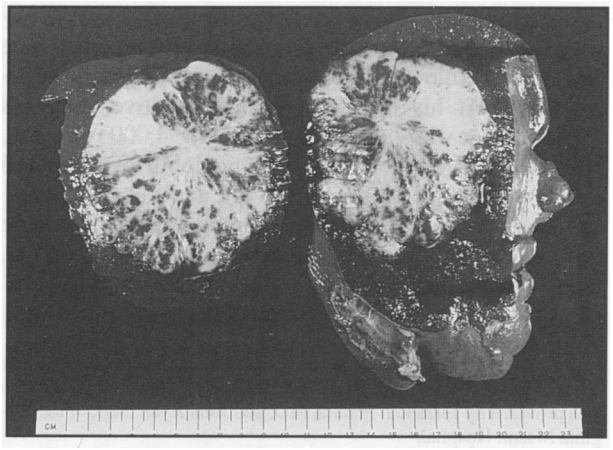

Figure 2.—The gross specimen of spleen, weighing 882 grams, contains a single expansile nodule 10 cm in diameter. Islands of dark (red) soft tissue are seen in a white, firm, fibrous-appearing stroma.

tomy during childhood. The incidence of fatal pneumococcal sepsis in adults is less, perhaps about 1 case per 1,000 patient-years. The risk is greater if the splenectomy was for malignant or hematologic disease rather than for trauma and is highest in the first few years after the procedure, although cases have occurred decades later. Primary bacteremia, sometimes complicated by meningitis, is the usual presentation, rather than a focal infection of the respiratory tract. Certain features occur in pneumococcal sepsis affecting asplenic hosts that are rarely, if ever, present in patients with spleens. These include disseminated intravascular coagulation, peripheral gangrene, hypoglycemia, and adrenal hemorrhage. The intensity of bacteremia is so great that organisms are sometimes visible on peripheral blood smears, indicating a concentration of about 10^6 bacteria per ml, compared with a level that rarely exceeds 200 bacteria per ml in patients with bacteremic pneumococcal pneumonia.[47] The mortality is about 60% to 70%, compared with about 20% in patients with bacteremic pneumococcal pneumonia. Patients with this disorder usually have nonspecific symptoms, such as fever, chills, sore throat, diarrhea, and myalgias, strongly suggesting a viral cause. Because pneumococcal sepsis is so frequently and rapidly fatal in asplenic hosts, clinicians should strongly suspect this possibility in those with an acute febrile disease, quickly obtain appropriate cultures, and institute antimicrobial therapy. Some authorities have recommended that asplenic patients have a supply of oral antibiotics to take immediately on having a febrile illness and then seek prompt medical attention. Some have also suggested regular penicillin prophylaxis, at least for the first few years after splenectomy in children, and preoperative administration of the pneumococcal vaccine, although its efficacy in these patients is unknown.

Splenectomy, therefore, imposes genuine immediate and long-term risks. In this patient, however, the clinical information does not allow a confident diagnosis of his underlying disease. This uncertainty, the possibility of a splenic malignant tumor, and the theoretical concern that an inflammatory pseudotumor, if present, could be premalignant support the plan for a diagnostic, and possibly therapeutic, splenectomy. Being a young and otherwise healthy adult, he has low risks for immediate postoperative complications, which are more common in older patients, and for later fulminant infections, which are much more frequent in children.

Clinical Diagnosis

Inflammatory pseudotumor of the spleen.

HENRY ROSEN, MD*: What was the opinion of the infectious disease consultants?

W. CONRAD LILES, MD, PhD†: Although parasitic diseases were still possible, we felt that this was most likely a benign tumor, probably of endothelial origin. We agreed with the recommendation for splenectomy and preoperative pneumococcal vaccination.

DR DRACHMAN: The patient underwent laparotomy and splenectomy at the Virginia Mason Hospital in Seattle. The pathologic evaluation will be presented by Susan Patterson, MD.

Pathology

SUSAN PATTERSON, MD‡: The spleen was 882 grams, $18 \times 12 \times 9$ cm, and smoothly encapsulated. It contained a single 10-cm-in-diameter expansile nodule (Figure 2). On the cut surface, the nodule was variegated, tan to red, rubbery, and partially calcified, with an ill-defined, irregular, nonencapsulated border pushing against uninvolved spleen.

On histologic examination, the tumor consisted of "granulomatous-appearing," poorly defined nodules of endothelial cells forming slit-like vascular spaces. Endothelial cells varied from plump and epithelioid to spindle-shaped. Intracytoplasmic lumens could be identified. Cells displayed no anaplasia or notable numbers of mitoses. Endothelial cells were strongly positive for factor VIII by immunoperoxidase studies. The stroma between nodules of endothelial cells was fibrotic with a mixed inflammatory infiltrate of lymphocytes, plasma cells, histiocytes, and occasional eosinophils (Figure 3).

This large splenic tumor is a neoplasm of partially epithelioid endothelial cells forming nodules of irregular vascular spaces. Vascular spaces are poorly formed centrally and surrounded by epithelioid endothelial cells, imparting a granulomatous appearance. Intervening stroma has a mixed inflammatory infiltrate and fibrosis. The slow growth is manifested by the central sclerosis and calcification. Overall features are those of a hemangioendothelioma, a tumor more commonly seen in soft tissue, liver, lungs, or bone. In fact, to my knowledge, no previous example of hemangioendothelioma in the spleen has been described.

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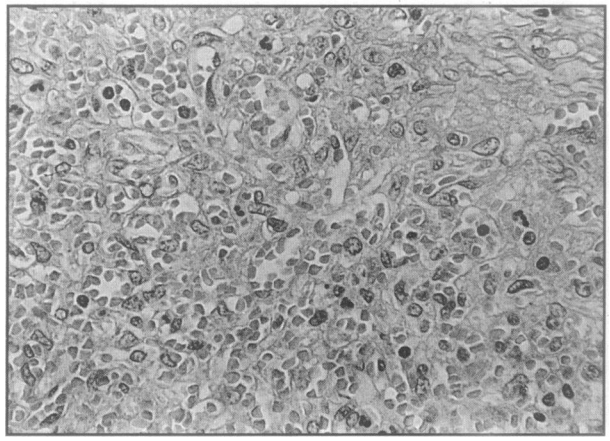

Figure 3.—On light microscopy, the irregular dark nodules seen grossly were composed of endothelial cells forming slit-like vascular spaces filled with erythrocytes (hematoxylin and eosin stain, original magnification × 250).

Hemangioendotheliomas are vascular tumors of endothelial origin midway between benign hemangiomas and angiosarcomas. Because of the epithelioid appearance of endothelial cells, these tumors can be mistaken for carcinoma or melanoma. Careful evaluation to identify the vasoformative cell pattern or immunoperoxidase studies to identify factor VIII are needed to recognize the true nature of these neoplasms. The behavior of the tumors varies greatly according to site of origin. In an organ such as the spleen that can be removed entirely, recurrence is unlikely. In other organs, such as bone, where the tumor is often multifocal, slow progression can occur. Surgical excision is the treatment of choice when possible.

The interpretation of this splenic nodule as an inflammatory pseudotumor was a reasonable diagnosis before histologic examination. Hemangioendotheliomas often have an inflammatory appearance, as this one does. When seen in soft tissue, the terms "angiolymphoid hyperplasia with eosinophilia" and "pseudopyogenic granuloma" have been used.

Histologic Diagnosis

Hemangioendothelioma of the spleen.

DR DRACHMAN: John Kirkpatrick, MD, has been the patient's primary care physician throughout his course. He will describe the patient's clinical condition since the surgical procedure.

JOHN KIRKPATRICK, MD*: The patient was discharged on the fifth postoperative day after an uneventful operation, except that his platelet count had risen to 603 × 10^9 per liter (603,000 per mm^3). He was readmitted a week later because of crampy lower abdominal pain and bloody stools. His platelet count on this admission was 975 × 10^9 per liter (975,000 per mm^3). A flexible sigmoidoscopy showed changes consistent with ischemic colitis; the patient was treated with hydroxyurea for this "postsplenectomy thrombocytosis." He was discharged after only one day, and on follow-up his platelet count has gradually diminished. At his three-month postoperative visit, his platelet count was 494 × 10^9 per liter (494,000 per mm^3), his hematocrit was 0.45 (45%), hemoglobin level was 146 grams per liter (14.6 grams per dl), and the ESR was 1 mm per hour. His energy has returned to normal, and he has not had any infectious complications. At this point, there is no evidence of recurrent or residual disease.

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